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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
BRUMBACK, B	
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DATE MAILED: 05/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/591,651	Applicant(s) Classen
	Examiner Brenda Brumback	Group Art Unit 1643

☒ Responsive to communication(s) filed on *Mar 25, 1999*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The amendment files 03/25/99 has been received and made of record as Paper # 10. Claims 2, 9, 14, 17, 21, 25, 31, 42, 45, 47, 53, and 54 were canceled. Claims 5, 6, 8, 10, 11, 15, 16, 26, 28-30, 32, 38, 48, and 50-52 were amended. New claims 56-101 were added. Pending claims are 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101. Claims 6, 32, 33, 56-58, and 101 are drawn to methods; claims 5, 8, 10, 11, 15, 16, 26-30, 34-41,43, 44, 46, 48-52, 55, and 59-100 are drawn to kits. Claim 19 is drawn to an immunogenic agent.

2. For clarification of the record, it is noted that claims 1, 3, 4, 7, 12, 13, 18, 23, and 24 were canceled during IPE.

Claim Rejections - 35 USC § 101/ Double Patenting

3. The rejection of claims 2-17, 19, 21, 23-33, and 34-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of Classen U.S. Patent No. 5,728,385 and claims 1-47 of Classen U.S. Patent No. 5,723,283 is maintained for claims 6, 32, and 33. Newly added claims 56-58, and 101 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of Classen U.S. Patent No. 5,728,385 and claims 1-47 or Classen U.S. Patent No. 5,723,283 for the reasons of record.

The rejection of claims 5, 8, 10, 11, 15, 16, 19, 26-30, 34-41, 43, 44, 46, 48-52, and 55 is withdrawn. Applicant's argument that the kit claims were restricted out in the parent case was persuasive.

Claims 2-4, 7, 9, 12-14, 17, 23-25, 31, 42, 45, 47, 53, and 54 have been canceled.

Claim Rejections - 35 USC § 112

4. The rejection of claims 2-17, 19, 21, 23-33, and 34-55 under 35 U.S.C. 112, first paragraph, is maintained for pending claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55. This rejection is also applied to newly added claims 56-101. Applicant's arguments have been fully considered but they are not persuasive for the following reasons.

a. Applicant argues that the specification is enabled for the broad scope of the claims because anthrax, plague and DT were shown to favorably affect diabetes and further argues that anthrax and DPT are very different. Applicant, however, does not elucidate what the significant differences are between anthrax and DPT (the examiner has assumed that "DT" is diphtheria/tetanus and that "DPT" is diphtheria/pertussis/tetanus). What the disclosure has shown is a reduction in the incidence of diabetes in a mouse model by administration of one or more of five bacterial immunogens (*Bacillus anthracis*, *Yersinia pestis*, *Corynebacterium diphtheriae*, *Bordetella pertussis*, and *Clostridium tetani*). This effect appears to be amplified when two or more of these antigens are administered together. The immunogens as claimed include a myriad of different viral antigens, as well as bacterial antigens. Applicant has not demonstrated the same

effect for viral immunogens absent bacterial proteins and lipopolysaccharides that has been demonstrated for the described bacterial antigens.

b. Applicant argues that the effectiveness of other immunogens is suggested by applicant's epidemiological data referring to immunization with BCG and smallpox. The disclosure teaches that BCG contains heat shock protein, which is a known toleragen that ameliorates certain immune diseases. This might reasonably be held as an alternative explanation for data indicating a possible correlation between reduction in diabetes mellitus and vaccination with BCG or other bacterial antigens. Furthermore, the epidemiological data presented in the disclosure is inconclusive because of differences in reporting incidence of diabetes among the study groups, differences in immunization protocols among the groups, fluctuations in immunization protocols within individual study groups, and differences in genetic predisposition for diabetes among the study populations, as well as other factors, such as the lack of controls inherent in any retrospective data analysis The actual incidence of diabetes in the populations studied is unknown, as diabetes is not a mandatory reportable disease in the populations evaluated.

c. Applicant's argument that the relationship between autoimmune disorders and microbial infections has nothing to do with the invention does not address the reason why the rejection was made; namely, that since the art of prevention of autoimmune disease is highly unpredictable and the mechanisms by which autoimmune diseases arise have not been elucidated,

it is thus unclear whether or not the full breadth of the claimed invention would have a positive effect in treating autoimmune disease.

d. The examiner acknowledges applicant's submission of the Classen Declaration previously submitted in parent case SN 08/104,529; however, the relevance of applicant's statement that only the pertussis and BCG vaccines have been shown to contain an immunogen that cross-reacts with an autoantigen associated with type I diabetes mellitus is not clear.

e. In response to applicant's arguments pertaining to the mechanism of action of the immunogens in preventing certain autoimmune disease, the disclosure contains only background information and hypotheses of proposed mechanisms of action, as is evidenced by the statement, "The immunization **may** act in several ways including ..." (emphasis added). No actual mode or modes of action have been determined and no definitive modes of action are taught in the disclosure.

f. Applicant's arguments pertaining to the uncertainty in the art as to the best age at which to vaccinate have been considered. While it is noted that the claimed methods do not require the affecting of an immune response to the immunogen, the intended use of the kits is stated as follows: "A kit for use to protect a mammal against an infectious disease to which a mammal is susceptible". This would certainly suggest its use for eliciting an immune response to the immunogen, as well as reducing the incidence or severity of a chronic immune-mediated disorder. Additionally, it remains unclear whether early immunization of infants can reduce the incidence or severity of an immune disorder. The working examples in the disclosure were

conducted using mouse or rat models; it is unclear if the data from the models would be applicable to human infants because of the differences in the growth and maturation rates of rodents compared to humans. The inherent pitfalls in accurate interpretation of epidemiological data have been addressed *supra.*

g. Regarding the rejection of the instant claims as lacking an enabling disclosure for treating autoimmune diseases commensurate in scope with the claims, applicant states "Disorders which are manifested through a common mechanism are likely to have a common cure or palliative". The plethora of autoimmune diseases known to occur in mammals are not known to share a common mechanism; rather, the art teaches that events leading up to development of autoimmune disease are complicated, vary from disease to disease, and are largely obscure. Therefore, it would not be expected that all autoimmune diseases would have a common cure or palliative, as applicant alleges. The single example of treating autoimmunity in MRL/lpr mice does not expand enablement from treating diabetes in a mouse model to treating all autoimmune diseases in all mammals, as is claimed.

h. Applicant's listing of two patents which have been issued claiming treatment of a large class of diseases while only showing examples of treating a single disease are not applicable to the instant application. Determination of enablement and patentability is based on the relevant statutes and on precedents set by case law, not on examples of other patents issued.

i. Regarding applicant's assertion that the data based on the mouse and rat models can be extrapolated to humans and other mammals because the animals used are accepted animal

models for human diabetes, applicant is reminded that in the instant case the extrapolation is in question because of the criticality of the age of administration of the immunogen and the differences in maturation rates between rodents and humans. The disclosure teaches that administration of an immunogen at certain times can actually exacerbate the development of diabetes mellitus. Because of the absolute criticality of the age of administration of the immunogen, there would not be a reasonable expectation of success in humans based on data from a mouse or rat model.

j. Applicant's arguments regarding the issue of determination of effective immunization schedules does not address the rejection. The rejection was based on the absence of any teaching in the disclosure of how to adjust the immunization schedule for the myriad of antigens that are claimed as "immunogens". For example, effective immunogenic compositions or vaccines against the HIV, HCV, and HSV viruses are not known in the art and are not available to the skilled artisan. If such immunogenic compositions are not known or readily available, then the disclosure must teach how to make them. Absent such a teaching, the skilled artisan would be unable to make or use the invention commensurate in scope with the claims. It would require undue experimentation to determine effective immunogens and immunization schedules for antigens which the art teaches are not immunogenic.

5. The rejection of claims 2-19 and 21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention is maintained for pending claims 5, 6, 8, 10, 11, 15, 16, and 19. Additionally, the rejection is applied to newly added claims 65-101. Applicant's arguments have been fully considered but they are not persuasive.

a. Applicant argues that "substantially greater" is not indefinite because the term "substantially" has been upheld in the courts when a suitable standard is disclosed. If this is so, then what is the "suitable standard" in the instant case? How much greater is "substantially greater". The examiner can find no standard taught in the disclosure for ascertaining this.

b. The definitions of "pediatric" and "nonpediatric" advanced in the specification are noted. Although the terms "pediatric" and "nonpediatric" are commonly used to describe the patient rather that the immunogen, the examiner withdraws this rejection in light of the list if immunogens which are classified in the disclosure as "pediatric" or "nonpediatric".

c. Applicant argues that function language is proper and customary in pharmaceutical method claims. However, the "function" as described in the instant claims is obscure and cannot be determined due to the inclusion of language such as "substantially". Therefore, the claims are indefinite.

d. Applicant argues that "other than BCG" is proper because one can disclaim a prior art species in a genus. For the exclusion to be proper, the other species of the genus must have been disclosed. In the instant case, "one immunogen other than BCG" does not define the metes and bounds of the other immunogens. Therefore, the claim is vague and indefinite.

e. The phrase "specific times after birth" renders the instant claims vague and indefinite because these specific times are not defined, nor are methods for determining specific times taught for the scope of the immunogens or mammals as claimed. Therefore, the skilled artisan would be unable to determine the metes and bounds of the invention as claimed.

Claim Rejections - 35 USC § 102

6. The rejection of claims 6, 21, 32, and 33 (method claims) under 34 U.S.C. 102(b) as being anticipated by Madore et al. is maintained. Applicant's arguments regarding the differences in the dosage schedules between Madore et al. and that of the instant claims as they are currently amended have been fully considered; however, the rejection is maintained because the amendment of claim 32 introduces new matter, as is discussed *infra*. Additionally , the rejection is applied to newly added kit claim 101.

7. The rejection of claims 8, 10, 11, 15, 16, 19, 26-30, 34-41, 43, 44, 46, 48-52, and 55 (kit claims) under 34 U.S.C. 102(b) as being anticipated by Madore et al. is also maintained. The rejection is also applied to new claims 59-100. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the labeling of the kit is that which distinguishes the claimed kits over those of the prior because printed matter is given patentable weight if there is a sufficient functional relationship between the printed matter and its substrate. The examiner maintains that there is no functional relationship between the printed labeling of the

claimed kits and any substrate. It is not even clear in the instant case what applicant intends to be the "substrate". Is the substrate the paper on which the instructions are printed? The citations set forth by applicant in support of this argument are not applicable to the instant case. In re Miller, 164 USPQ 46 pertains to a mathematical device wherein the printed matter (numbers) define the function of the device; similarly, In re Gulack 217 USPQ 401 pertains to a measuring cup, wherein the function of the apparatus depends on the printed numbers on the substrate. No such relationship is found in the instant case. The labeling simply defines an intended use for the claimed kit and thus is not given patentable weight.

8. The rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 under 35 U.S.C. 102(b) as anticipated by Dengrove et al. is maintained; the rejection is also applied to new claims 56-101, for the reasons outlined *supra*.

9. The rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 under 35 U.S.C. 102(b) as anticipated by Halsey et al. is maintained: the rejection is also applied to new claims 56-101, for the reasons outlined *supra*.

10. The rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 under 35 U.S.C. 102(b) as anticipated by John is maintained: the rejection is also applied to new claims 56-100, for the reasons outlined *supra*.

11. The rejection of claims 26, 27, 34-36, 38-41, 43, 44, and 46 under 35 U.S.C. 102(b) as anticipated by Chazono et al. is maintained: the rejection is also applied to new claims 56-100, for the reasons outlined *supra*.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

12. Claims 6, 32, and 101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent claims 32 has been amended to recite additional limitations which do not find support in the instant specification. The examiner has considered applicant's statement that certain of the limitations are copied from a claim of issued patent 5,728,385, issued on parent case 08/104,529; however, the instant case is a continuation-in-part of the parent case. Continuity between the parent and child cases has not been established. Neither has the specification of the parent application been incorporated herein by reference. Therefore, the newly added limitations do not find support in the parent disclosure. This matter might by resolved if applicant were to point out where in the instant specification or in the originally disclosed parent specification support for the newly recited material may be found.

13. Claims 5, 8, 10, 11, 30, 38, 49, 55, 60, 61-65, 72-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Independent claim 59 has been amended to recite "a kit for use to protect a mammal against an infectious disease to which a mammal is susceptible...". The art teaches that immunogenic compositions cannot give absolute protection against the infectious agent. The examiner notes applicant's argument that the disclosure teaches "protecting against an infectious disease" on page 47 as conferring "a beneficial clinical effect" and applicant's statement that "protection is a matter of degree"; however, protection implies an absolute, not a matter of degree. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947).

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Chris Eisenschenk whose telephone number is (703) 308-0452. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1643 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1643 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
April 28, 1999

DONNA WORTMAN
PRIMARY EXAMINER